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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,582	03/04/2002	Guixue Yu	HA0768 NP	5031

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EXAMINER

CHANG, CELIA C

ART UNIT	PAPER NUMBER
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1625

DATE MAILED: 05/07/2003

6

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Applicati n N .

10/090,582

Applicant(s)

YU ET AL.

Examiner

Celia Chang

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-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 14 January 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 9,19 and 20 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☐ Claim(s) 1-8,10-16,18,21 and 22 is/are rejected.
- 7) ☐ Claim(s) 17 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 & 5. 6) ☐ Other:

DETAILED ACTION

1. Claims 1-22 are in the case.

2. *Restriction*

Restriction to one of the following inventions is required under 35 U.S.C. 121:

- I. Claim 9, drawn to XR1CHR2CHR3CH2 forms a ring compound, classified in class various, subclass various. If this group is elected a further election of a single disclosed species is also required. The claims will be further restricted based on the structure of claim 9. Generic claims 1, 3-8, 10-15, 18, 21-22 reading on the elected compound can be prosecuted together with the elected compounds to the extend of the election.
- II. Claims 2, 16-17, drawn to piperidinyl compounds, classified in class 546, subclass various, depending on species election. Generic claims 1, 3-8, 10-15, 18, 21-22 reading on the elected compound can be prosecuted together with the elected compounds to the extend of the election.
- III. Claims 1, 3-8, 10-15, 18-22, drawn to remaining compounds ($z=0$ or 2), classified in class various, subclass various. If this group is elected a further election of a single disclosed species is also required. The claims will be further restricted based on the elected species being z is 0 or 2. Generic claims 1, 3-8, 10-15, 18, 21-22 reading on the elected compound can be prosecuted together with the elected compounds to the extend of the election.
- IV. Claims 19-20, drawn to multiple active ingredient composition, classified in class various, subclass various depending on species election. If this group is elected, a further election of a single combination of a compound of claim 1 with another single active compound is also required. Further restriction may be required.

The inventions are distinct, each from the other because:

Compounds of groups I-III differ in elements, chemical bonding arrangement and chemical properties to such an extend that a reference anticipating compounds of any one group would not render claims of another group of compounds obvious. The search for each group is

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not coextensive and proper classification can not be made without a species election. Not only each group compounds can support its own patent, but also it would be a tremendous burden to search all structural diverse compounds without restriction.

A multiple ingredient composition of group IV is not related to compounds per se since patentability of a multiple ingredient composition depends on the active ingredient and their respective dosage in the composition. Separate search and examination are required.

During a telephone conversation with Anastasia Winslow on Jan. 30, 2003 a provisional election was made with traverse to prosecute the invention of group II, claims 2, 16-17 and generic claims 1, 3-8, 10-15, 18, 21-22 reading on claim 2 compounds. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9, 19-20 and claims 1, 3-8, 10-15, 18, 21-22 being drawn to non-piperidinyl compounds or XR1CHR2CHR3CH2 forms a ring compound are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Should applicant traverse on the ground that the groups and species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the groups and species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

3. There are empty spaces with information not disclosed in the specification for example on pages 4 and 16 the serial numbers are missing. Applicants are requested to check the specification and provide all pertinent information thereof.
4. Claims 1-6, 12-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for prodrugs such as acylation of the free amino functionality

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or fused heterocyclic ring such as delineated on pages 16-17, does not reasonably provide enablement for the scope as claimed encompassing any and all prodrug or indefinite fused ring structure. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims

Please note that the term “prodrug” can encompass from single acylation to convoluted preparation such as prolong release targeted conjugate etc. for which antecedent basis or enabling description are lacking.

Please note that the term “wherein two.....are joined to form a fused ring” has been used multiple times to describe chemical structure is ambiguous and indefinite. It must be clearly described in the structural definition before one skilled in the art can decide whether starting material for making is available. Starting material is of critical importance when at the point of novelty. Without starting material or description thereof, the public is offered mere language than description or enablement. In re Moersch 104 USPQ 122, In re Howarth 210 USPQ 689.

5. Claims 21-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating pathology/disease which are caused by deficiency of melanocortin receptor function, does not reasonably provide enablement for the claimed scope in treating condition “associated with” melanocortin receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to operate the invention commensurate in scope with these claims.

Please note that a compound can either be a melanocortin receptor antagonist *or* a melanocortin receptor agonist but can not be simultaneously function in both way which are opposite of each other. Therefore, a single compound can either treat diseases that require enhancement of the receptor function *or* inhibition of the receptor function but not both. Therefore, the claims being drawn to treating melanocortin-receptor associated condition can not be achieved since simultaneous inhibit and enhancing of the receptor function by a single compound can not be attained. The claims should be particularly pointed to the specific conditions which are treatable by the compound per se.

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6. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is self conflicting because it is a pharmaceutical composition without dosage limitation. A pharmaceutical composition must not be ineffective or toxic. Therefore, it is recommended that the "therapeutically effective amount" of the active ingredient be incorporated into the claims.

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-2, 4-5, 7-8, 10, 14, 18 and 21-22 are rejected under 35 U.S.C. 102(e) as being anticipated by Palucki et al. US 6,458,790.

See claims 1-29, col. 212-290 anticipated the instant claims wherein W is piperazinyl optionally substituted, or optionally fused.

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459

(1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-2, 4-8, 10, 12-14, 18, and 21-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Palucki et al. US 6,458,790.

Determination of the scope and content of the prior art (MPEP §2141.01)

Palucki et al. '790 disclosed compounds which anticipated the broad claims as pointed out supra.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Palucki et al. '790 disclosed all the elements of the claims **except** a species wherein one of R8 or R9 being cycloalkyl and heteroarylalkyl while W is piperazine has not been exemplified.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would be motivated to modify the anticipatory species with guidance in other examples since all compounds exemplified have similar activity as taught generically by Palucki '790 and explicitly enabled in alternative compounds (see co.155-156 compound 111). The instant claims being drawn to the modification of a proven compound with attribute of another example for the Markush group of the prior art is prima facie obvious.

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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Claims 1-5, 7-8, 10-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morriello et al. US 5,622,973 in view of Hansen et al. US 6,303,620.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35

U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Determination of the scope and content of the prior art (MPEP §2141.01)

Morriello et al. '973 disclosed structural similar compounds of the claims and explicitly disclosed compounds on col. 145-147 which are structural analogous and have growth hormone secreatage activity.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Morriello et al. '973 disclosed all the elements of the claims **except** compounds disclosed at col. 145-147 are substituted by R8 and R9 at the 3-position of the piperidiny ring while the instant claims are drawn to 4-substitution compounds. Hansen et al. '620 is analogous art in growth hormone secreatage compounds wherein it was taught that both 3- and 4- substitution are obvious variation with expected similar activity (see col. 35-36 examples 10-13).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art is deemed to be aware of all the pertinent art in the field. The above references place the skill of making growth hormone secreatage compounds being 3- or 4-substituted piperidine in the possession of artisan in the field. The modification of a proven compound with attributes of another proven compound is considered prima facie obvious **because** position isomerism (over Morriello '973) is well established as prima facie structurally obvious (In re Mehta 146 USPQ 284), and analogous art explicitly suggested to one skilled in the art that not only position isomeric compounds can be made but also the reasonable expectation of such isomers to have similar art recognized activity (evidenced by Hansen '620).

10. Claim 17 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

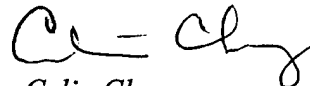
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11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

*OACS/Chang
May 1, 2003*



*Celia Chang
Primary Examiner
Art Unit 1625*